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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,625	12/22/2003	Arthur M. Krieg	C1039.70073US00	9416

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
07/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/743,625	KRIEG ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment filed April 10, 2007 is acknowledged and has been entered. Claims 1-18 have been canceled. Claims 19-39 are now pending in the present application. All rejections have been withdrawn in view of Applicants' comments with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 19-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42-47, 49-53, 56, 57, 82-85, 90, 92, 94, 96, 98, 100, 102 and 103 of copending Application No. 09/337584. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications recite claims directed to a method for treating asthma in a subject, comprising administering to the subject an effective amount for treating asthma in the subject of an immunostimulatory oligonucleotide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 19-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 46, 52, 64, 71, 72, 74 and 80 of copending Application No. 10/613739. Although the conflicting claims are not identical, they are not patentably distinct from each other

because both applications recite claims directed to a method comprising administering to the subject an immunostimulatory oligonucleotide. Although 10/613739 does not recite treatment for asthma, this would be the result since the methods steps are the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 19-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22, 23, 31, 32 and 34-37 of copending Application No. 10/769282. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications recite claims directed to a method comprising administering to the subject an immunostimulatory oligonucleotide. Although 10/769282 does not recite treatment for asthma, this would be the result since the methods steps are the same. Application 10/769282 recites a method of modulating an immune response, the administration of the immunostimulatory oligonucleotide modulates a Th1 immune response, which is the immune response modulated in an asthmatic subject that has received the immunostimulatory oligonucleotide.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6 Claims 19-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-29 and 31-33 of copending Application No. 10/894862. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications recite claims directed to a method comprising administering to the

subject an immunostimulatory oligonucleotide. Although 10/894862 does not recite treatment for asthma, this would be the result since the methods steps are the same. Application 10/894862 recites a method of inducing a Th1 immune response and suppressing a Th2 immune response, the administration of the immunostimulatory oligonucleotide modulates a Th1 immune response, which is the immune response modulated in a asthmatic subject that has received the immunostimulatory oligonucleotide; the Th2 immune response is suppressed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 19-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42, 45-53, 57-60 of copending Application No. 09/337893. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications recite claims directed to a method comprising administering to the subject an immunostimulatory oligonucleotide. Although 09/337893 does not recite treatment for asthma, this would be the result since the methods steps are the same. Application 09/337893 recites a method for redirecting a subject's immune response from a Th2 to a Th1 immune response, the administration of the immunostimulatory oligonucleotide modulates a Th1 immune response, which is the immune response modulated in an asthmatic subject that has received the immunostimulatory oligonucleotide; the Th2 immune response is suppressed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. The provisional obviousness-type double patenting rejection over 09/337584, 10/613739, 10/769282, 10/894862 and 0/337893 is maintained. Applicants' arguments filed April 20, 2007 have been fully considered but they are not persuasive. Applicants have asserted that the rejections are provisional since none of the claims in the 09/337584,10/613739, 10/769282, 10/894862 and 0/337893 applications have been found allowable. If any of the cited claims are found allowable, Applicants will address the rejection.

It is noted that Applicants did not address the provisional ODP rejection over 10/769282.

10. Claims 19-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims recite "...an immunostimulatory oligonucleotide comprising an immunostimulatory motif comprising a 5'-cytosine-guanine-3'...".

The claims do not define the structure of the immunostimulatory oligonucleotide comprising an immunostimulatory motif comprising a 5'-cytosine-guanine-3'. What is the exact structure of the immunostimulatory oligonucleotide? The claims only recite that it must contain a 5'-cytosine-guanine-3'. The structure is not defined.

The structure of the immunostimulatory oligonucleotide is vast in view of the recitation of the open claim language of "comprising". Further, it is noted that

neither the specification nor the claims disclose the structure of the oligonucleotide set forth in the claims. The recitation of comprising indicates that there are other structural components to the claimed immunostimulatory oligonucleotides and these the structures of the additional nucleic acids in the immunostimulatory oligonucleotides are not known. The immunostimulatory oligonucleotides recited in the pending claimed genus would not clearly apprise one skilled in the art that the inventors had possession of the claimed genus and all species encompassed thereby as of the filing date. The structure of these immunostimulatory oligonucleotides has not been specifically defined. The claims do not set forth the specific structure of the claimed immunostimulatory oligonucleotides and it is not clear if the claims or specification give the structure and a function of the immunostimulatory oligonucleotides, as required by the written description guidelines.

A review of the specification discloses a list of immunostimulatory nucleic acids that could be used in the claimed invention. However, they comprise 8 or more nucleotides (see for example Tables 1, 2, 5, 9, 10), not the 6 nucleotides as set forth in claim 19. It is noted that Applicants' specification indicates that ODNs shorter than 8 bases were non-stimulatory (p. 19, l. 4-5).

The state of the art is unpredictable with regard to the use of oligonucleotides of less than 8 nucleotides having immunostimulatory activity.

Yamamoto et al 1994 (Antisense Research and Development, 1994, 4 :119-122) teaches that "immunostimulatory activity of oligonucleotides 18 bases or more in length was observed and was proportional to the base length, with a maximum at 22-30 bases. On the other hand, the oligonucleotides 16 bases or less in length were not as active even if they possessed the palindromic sequences.

These results indicate that the immunostimulatory activity of oligonucleotides with certain palindromic sequences requires an oligonucleotide at least 18 bases long." (abstract).

It is noted that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed.

A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific

example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original); Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

The claims are drawn to a vast genus of immunostimulatory oligonucleotides. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of

the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics

sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it.") (emphasis in original). In Ex parte Ohshiro, 14 USPQ2d 1750 (Bd. Pat. App. & Inter. 1989), the Board affirmed the rejection under 35 U.S.C. 112, first paragraph, of claims to an internal combustion engine which recited "at least one of said piston and said cylinder (head) having a recessed channel." The Board held that the application, which disclosed a cylinder head with a recessed channel and a piston without a recessed channel did not specifically disclose the "species" of a channeled piston.

The rejection is maintained for the reasons of record. Applicant's arguments filed April 10, 2007 have been fully considered but they are not persuasive. Applicants have asserted that the ODNs of the invention are not described merely by functional characteristics. The ODNs of the invention are described by structure, formula, name, and physical properties - as ODNs with specific sequences, specific lengths, and specific internucleotide linkages. In addition, modifications to the bases, nucleosides, and the linkages as envisaged by the instant invention are also described. Examples of specific sequences, linkages and structures of the oligonucleotides of the instant invention are shown the summary of the invention and the detailed description.

It is noted that the claims recite the open claim language of "comprising" and therefore it is not clear what the exact structure of the claimed ODN is. Claim 19 only recites a structure of a CG. The claims only give a specific length of 2 nucleotides, however, the specification and the state of the art teaches that the minimum length for immunostimulatory activity is 8 nucleotides. It is noted that Applicants' specification indicates that ODNs shorter than 8 bases were non-stimulatory (p. 19, l. 4-5). The state of the art is unpredictable with regard to the use of oligonucleotides of less than 8 nucleotides having immunostimulatory activity. Yamamoto et al 1994 (Antisense Research and Development, 1994, 4 :119-122) teaches that "immunostimulatory activity of oligonucleotides 18 bases or more in length was observed and was proportional to the base length, with a maximum at 22-30 bases. On the other hand, the oligonucleotides 16 bases or less in length were not as active even if they possessed the palindromic sequences. These results indicate that the immunostimulatory activity of oligonucleotides with

certain palindromic sequences requires an oligonucleotide at least 18 bases long." (abstract). The rejection is maintained for the reasons of record.

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN US OR CANADA) or 571-272-1000.

N. M. Minnifield
Primary Examiner
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NMM

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